

# Defeating Air Pollution: Unraveling the Pathogenic Mechanism of PM<sub>2.5</sub>

Aerosols, referring broadly to ultrafine particulate matter (PM) suspended in a gaseous medium, are found to play increasingly important roles in atmospheric chemistry, environmental science, public health and biomedical sciences in the past five years; see Fig. 1 for correlations of aerosol science with various associated research fields.

Although naturally produced aerosols are essential to maintain the radiative balance for Earth, anthropogenic aerosols produced from various human activities, such as industrial processes, transport emissions and coal burning have severely disturbed the homeostasis of Earth's environment. These unnaturally produced aerosols have altered the microphysics of the formation and growth of clouds, altered atmospheric photochemical processes, worsened air quality and caused marked adverse health effects for human beings. As reported by the International Agency for Research on Cancer of the World Health Organization (WHO), exposure to ambient fine PM in polluted air contributed to 3.2 million premature deaths worldwide in 2010; amongst them 223,000 mortalities were due to lung cancers.<sup>1</sup> In an updated WHO report released in 2014, the mortalities associated with exposure to air pollution increased to 7 million in 2012, accounting for 1/8 of total global deaths. These findings stress unambiguously the facts that air pollution and the PM suspended therein have become the largest environmental factor contributing to human health risk and mortality. Among all PM suspended in the air, PM<sub>2.5</sub>, which is defined as PM with an aerodynamic diameter smaller than 2.5  $\mu\text{m}$ , are particularly harmful to human bodies. While large PM (> 2.5  $\mu\text{m}$ ), once inhaled might be removed by lung mucous and cilia, PM<sub>2.5</sub> can penetrate to the alveolar, the deepest region of the lung in which occurs an exchange of gas between air and blood, or even enter the systemic circulation to cause further adverse health effects.

Even though the correlations between PM<sub>2.5</sub> and various morbidities, including pulmonary and lung diseases, cardiovascular diseases and cancers, have been well established from epidemiology studies, their pathogenic mechanisms remain elusive at the molecular level. The reason is mainly that our understanding of the fundamental physical, chemical and biological properties of PM<sub>2.5</sub> as well as of the biomolecules that are vulnerable to attack by PM<sub>2.5</sub>, is insufficient. Among varied intrinsic characteristics, the valence-electronic structure and ionization energy of a substance are especially crucial as these properties decisively determine the chemical activities of the substance with other chemical species. Whereas the valence electronic properties of PM<sub>2.5</sub> might depend critically on the size, shape, composition and internal architecture, the valence-electronic properties of a biomolecule might also rely crucially on the aqueous environment in which they reside and conduct their biological functions, through the pronounced solvent-solute interaction and hydrogen-bond effect.

With the objective to understand the valence- electronic

properties of both PM<sub>2.5</sub> and the biomolecules that are likely vulnerable to be affected by PM<sub>2.5</sub>, and eventually to clarify the pathogenic mechanism of PM<sub>2.5</sub> in leading to various morbidities, a research team led by Chia C. Wang of National Sun Yat-Sen University has recently developed a novel apparatus to record the VUV photoelectron spectra of aerosols; this spectrometer is capable of measuring the valence-electronic structural properties of both PM<sub>2.5</sub> and solvated biological molecules, as shown in Fig. 2.<sup>2</sup> The VUV radiation generated via undulator U9, at BL21B2, served as the ionization source. The usage of VUV plays a determining role in the experiments on photoelectron spectra of aerosols as it provides a soft mechanism for ionization, allowing the valence-level electronic structures of target aerosol species and their electronic evolutions to be measured, rather than the core-level electrons typically measured in X-ray photoelectron spectra.

In this featured work, Wang and her research team have chosen a unique and biologically important amino acid, cysteine (Cys), to study its valence-electronic properties and the evolution in its aqueous aerosol form, and in so doing to demonstrate the strength of the newly constructed apparatus. Through the active thiol (-SH) group at its side chain, Cys is highly nucleophilic and generally plays a key role in many important redox-based biological processes, including mediating the signaling paths and regulating the activi-

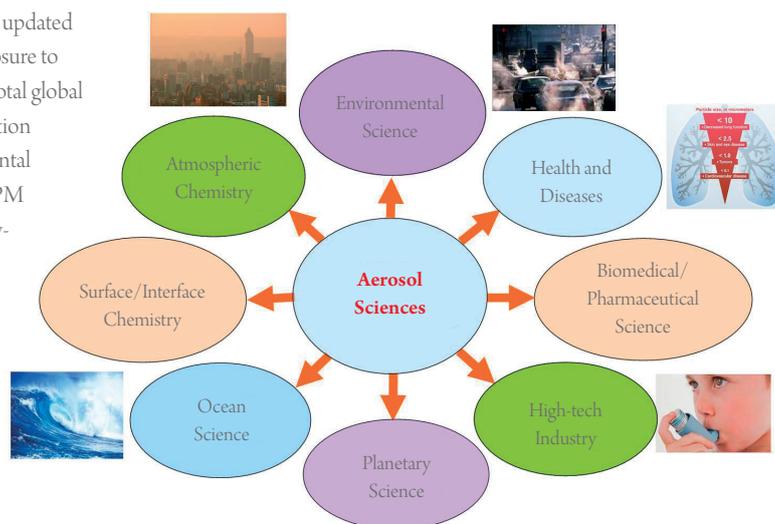


Fig. 1: Illustration of the correlations of aerosol science with several important fields.

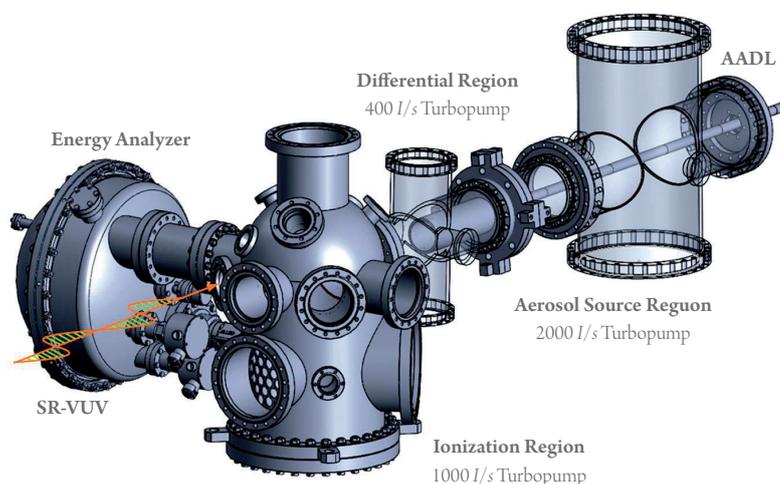


Fig. 2: Schematic view of the aerosol VUV photoelectron spectroscopy apparatus. The polarization vector of SR-VUV (BL21B2) is specified. [Reproduced from Ref. 2]

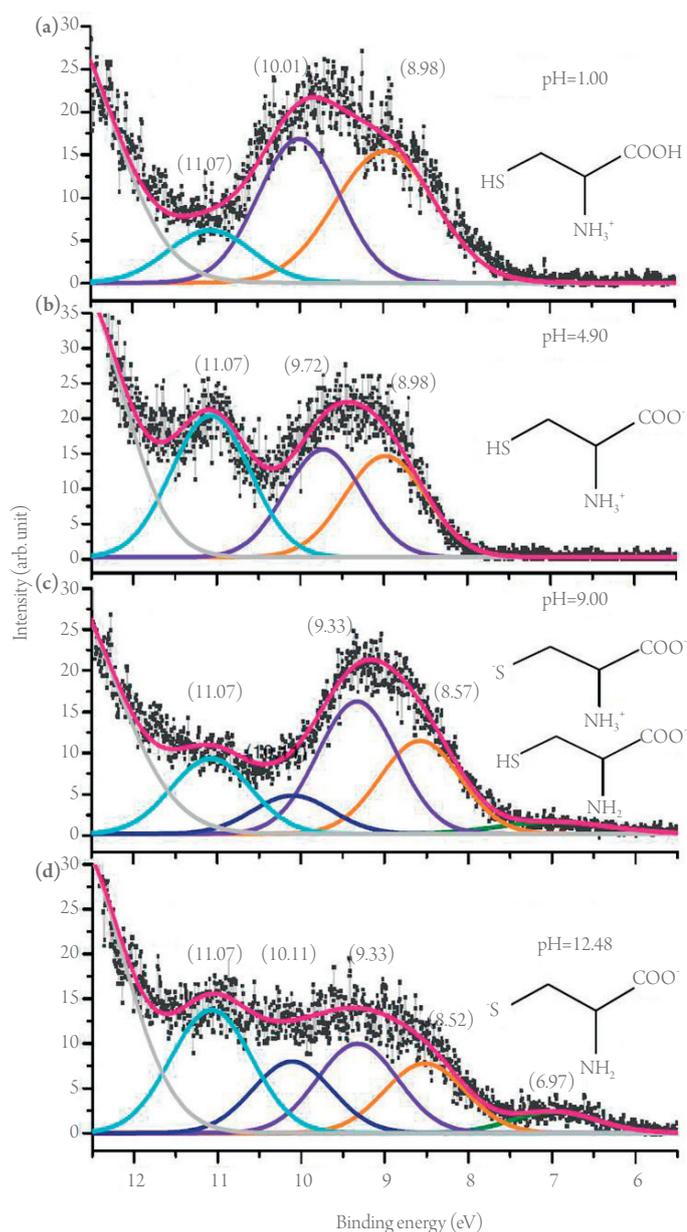


Fig. 3: VUV photoelectron spectra of Cys aqueous aerosols at four chosen pH conditions measured at 25 eV. A. pH = 1.00, B. pH = 4.90, C. pH = 9.00 and D. pH = 12.48. Symbols: experiment,  $\blacksquare$ ; Cys  $n_s$ , green curve; Cys  $n_\alpha$ , orange curve; Cys  $n_\beta$ , violet curve; Cys  $n_\gamma$ , blue curve; condensed water, cyan curve; gaseous water (only partial), grey curve; cumulative curve, pink curve. [Reproduced from Ref. 2]

ties of enzymes via S-nitrosylation and thiol oxidation. Despite the biological significance, the valence electronic properties of Cys in aqueous environments were unavailable before this work.

In this featured work, Cys was introduced into the aqueous aerosol phase of size  $\sim 100$  nm, which readily created a bulk aqueous environment on a nanometre scale, allowing the valence-electronic properties of Cys and its possible evolution with altering aqueous environments to be studied in a systematically controlled way. Because Cys exhibits three possible sites of deprotonation, these varied forms of protonation and deprotonation are dominant at varied pH values. To learn how the valence-electronic properties of Cys are affected by the altering local chemical environments or by the varying nature of its charged status, Prof. Wang and coworkers measured VUV photoelectron spectra of Cys aqueous aerosols at selected values pH = 1.00 (Fig. 3(a)), 4.90 (Fig. 3(b)), 9.00 (Fig. 3(c)) and 12.48 (Fig. 3(d)) at 25 eV, with each pH

condition representing a major chemical species. The photoelectron spectra of Cys aqueous aerosols in the four aqueous conditions explicitly show distinct photoelectron band shapes, reflecting the modified molecular-orbital character of Cys as the local chemical environment varies with pH. The ionization energy of Cys in an aqueous solution of small pH has been determined for the first time to be  $8.98 \pm 0.05$  eV. It is notable that a new spectral feature was observed at pH = 9.00 and 12.48 with a smaller binding energy,  $6.97 \pm 0.05$  eV, indicating that the negative charge on the thiolate group becomes the first electron to be removed upon ionization. The results reported in this featured work provided a new microscopic perspective to understand the nucleophilicity of Cys at varied pH. The authors showed that Cys loses an electron more easily with increasing pH, and a new ionization channel with a smaller energy barrier becomes open when the thiol group is deprotonated. As outlined in Marcus's charge-transfer (CT) theory, this result implies that, when Cys is involved in a redox process, the CT path might be entirely altered when its local chemical environment varies with pH, and accordingly the rate and efficiency of CT. The results illustrated in this work consequently provide valuable hints to enable one to understand how the biochemical activity of Cys becomes affected when the active and oxidizing components of PM2.5 interact with the highly nucleophilic Cys upon inhalation. From a more general perspective, this featured work provides an elegant example to demonstrate how sensitively the valence-electronic properties of an aerosol can be affected by its local chemical environment.

This novel VUV aerosol technique presents valuable and promising opportunities to study fundamental and important properties of both aerosols and solvated biological molecules in an aqueous aerosol form, and to address critical issues regarding PM2.5 and its related fields, including environmental science, atmospheric chemistry and biomedical science. We remark additionally that the authors in this featured work demonstrated elegantly also the power of using of the new approach to record photoelectron spectra of an aqueous aerosol so as to probe solvated species, and its advantages over the conventional liquid microjet technique. By overcoming the electrokinetic charging issue that is typically encountered in the liquid microjet technique and by considerably improving the spectral resolution, detailed insight regarding the solvated species and the aerosols can be expected to be unraveled via this newly developed approach. In the near future, Wang and her research team are planning to investigate more environmentally important PM2.5, with a focus on clarifying the fundamental mechanisms underlying the adverse impacts of PM2.5 on human health at a molecular level. (Reported by Yin-Yu Lee and Chia-Chen Wang)

*This report features the work of Chia-Chen Wang and her co-workers published in J. Phys. Chem. Lett. 6, 817 (2015).*

#### References

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2. C.-C. Su, Y. Yu, P.-C. Chang, Y.-W. Chen, I. Y. Chen, Y.-Y. Lee, and C. C. Wang, *J. Phys. Chem. Lett.* **6**, 817 (2015).